REMARKS

Claims 56-71 and 73-84 are now pending. Claims 67, 68 and 70 have been amended, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents.

No new matter is added.

It is respectfully submitted that the amendment to the claims is not made for the purpose of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112; but rather the amendments herewith are made simply for clarification and to round out the scope of protection to which Applicants are entitled.

The February 24, 2003 Communication stated that the amendment filed December 9, 2002 did not comply with all the requirements of 37 C.F.R. §1.121(c) because claims 67, 68 and 70 contained discrepancies between the clean copy of the claims and the marked-up version.

These discrepancies are corrected herein, and the amendments to claims 67, 68 and 70 are represented for consideration and entry.

Prior to issuance of any paper other than a Notice of Allowance, the Examiner is respectfully invited and requested to telephonically contact the undersigned so that the Examiner and the undersigned may conduct a further interview, with supervisory review if necessary, with a view towards reaching agreement on allowable subject matter, especially as expediting prosecution and reaching agreement with the Examiner on allowable subject matter are desired.

Respectfully submitted,

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MARKED VERSION OF AM

IN THE CLAIMS

67. (Amended) [A] The method for breaking B-cell autotolerance [illegible] self-protein of that animal, and inducing antibody production in the animal against the [illegible] a protein of that animal of claim 66 wherein the T-cell epitope comprises at least 10 amino ac[illegible] comprising administering to the animal, an immunologically effective amount of at least one modified self-protein, wherein:

the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self- protein, by being detoxified and by containing a substitution of at least one peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, said substitution preserving secondary and tertiary structure of the self-protein,

whereby the modified self-protein elicits antibodies that are against the self-protein, and B-cell autotolerance to the self-protein is broken.]

68. (Amended) A method for breaking B-cell autotolerance in an animal to a self-protein of that animal, and inducing antibody production in the animal against the self-protein of that animal, comprising;

preparing different modified self-proteins, wherein:

each modified self-protein is modified, in comparison to the self-protein, by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal,

[said substitution preserving tertiary structure of the self-protein,] and

the different modified self-proteins differ from each other with respect to the position of the at least one immunodominant T-cell epitope;

ascertaining which of the different modified self-proteins elicits a desired specific neutralizing effect and thereby ascertaining a desired modified self protein; and

administering to the animal, an immunologically effective amount of the desired modified self-protein, wherein:

the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein, and,

the desired modified self-protein elicits antibodies that are against the self-protein, and B-cell autotolerance to the self-protein is broken.

70. (Amended) A method for breaking B-cell autotolerance in an animal to a self-protein of that animal, and inducing antibody production in the animal against the self-protein of that animal, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes, comprising administering to the animal, an immunologically effective amount of at least one modified self-protein, wherein:

a. the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, wherein the peptide fragment corresponds to the peptide containing at least one immunodominant T-cell epitope in amino acid length [said substitution preserving tertiary structure of the self-protein];

whereby, the modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes, and B-cell autotolerance to the self-protein is broken; or,

b. the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, wherein the substitution is of an amphiphatic alpha helix [said substitution preserving secondary and tertiary structure of the self-protein];

whereby the modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes, and B-cell autotolerance to the self-protein is broken; or,

c. the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, wherein the peptide fragment corresponds to the peptide containing at least one immunodominant T-cell epitope in amino acid length and comprises [said substitution preserving tertiary structure of the self-protein, and said substitution preserving flanking regions comprising] at least [four] ten amino acids [on each side of the peptide fragment];

whereby the modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes, and B-cell autotolerance to the self-protein is broken; or,

d. the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, wherein the peptide fragment corresponds to the peptide containing at least one immunodominant T-cell epitope in amino acid length and comprises [said substitution preserving tertiary structure of the self-protein, and said substitution preserving flanking regions comprising] at least [ten] fifteen amino acids [on each side of the peptide fragment];

whereby the modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes, and B-cell autotolerance to the self-protein is broken; or,

e. the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, wherein the peptide fragment corresponds to the peptide containing at least one immunodominant T-cell epitope in amino acid length and comprises at least 10 amino acids with [said substitution preserving tertiary structure of the self-protein, and] said substitution preserving flanking regions comprising at least [fifteen] four amino acids on each side of the peptide fragment,

whereby the modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes, and B-cell autotolerance to the self-protein is broken; or,

f. the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal[, said substitution preserving tertiary structure of the self-protein], wherein the peptide fragment corresponds to the peptide containing at least one immunodominant T-cell epitope in amino acid length and comprises at least 15 amino acids with said substitution preserving flanking regions comprising at least four amino acids on each side of the peptide fragment,

whereby the modified self-protein elicits antibodies that are against the self-protein earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes; [and, the modified self-protein elicits an immune response in the animal which includes an MHC class II immune response as to the immunodominant T-cell epitope and an autoantibody response in other MHC-haplotypes,] and B-cell autotolerance to the self-protein is broken; or,

g. the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by being detoxified [and] by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, [said substitution preserving tertiary structure of the self-protein,]

whereby the modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes, and B-cell autotolerance to the self-protein is broken; or,

h. the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by being detoxified by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, [said substitution preserving secondary and tertiary structure of the self-protein,] and said substitution preserving [secondary and tertiary structure of the self-protein, and said substitution preserving] flanking regions comprising at least four amino acids on each side of the peptide fragment;

whereby the modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes, and B-cell autotolerance to the self-protein is broken; or,

i. the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by being detoxified by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, [said substitution preserving secondary and tertiary structure of the self-protein,] wherein said peptide containing at least one immunodominant T-cell epitope comprises at least 10 amino acids and said substitution [preserving] preserves flanking regions comprising at least [ten] four amino acids on each side of the peptide fragment;

whereby the modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes, and B-cell autotolerance to the self-protein is broken; or,

j. the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self-protein, by being detoxified by containing a substitution of [at least one] a peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, [said substitution preserving secondary and tertiary structure of the self-protein,] wherein the peptide containing at least one immunodominant T-cell epitope comprises at least 15 amino acids and said substitution [preserving] preserves flanking regions comprising at least [fifteen] four amino acids on each side of the peptide fragment,

whereby the modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes, and B-cell autotolerance to the self-protein is broken.[; or,]

[k. the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self- protein, by containing a substitution of at least one peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, said substitution preserving secondary and tertiary structure of the self-protein,

whereby the modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes; and, the modified self-protein elicits an immune response in the animal which includes an MHC class II immune response as to the immunodominant T-cell epitope and an autoantibody response in other MHC-haplotypes, and B-cell autotolerance to the self-protein is broken; or,

1. the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein; and,

the modified self-protein is modified, in comparison to the self- protein, by being detoxified and by containing a substitution of at least one peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal, said substitution preserving secondary and tertiary structure of the self-protein,

whereby the modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes, and B-cell autotolerance to the self-protein is broken; or,

m. preparing different modified self-proteins, wherein:

each modified self-protein is modified, in comparison to the self- protein, by containing a substitution of at least one peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal,

said substitution preserving tertiary structure of the self-protein, and

the different modified self-proteins differ from each other with respect to the position of the at least one immunodominant T-cell epitope;

ascertaining which of the different modified self-proteins elicits a desired specific neutralizing effect and thereby ascertaining a desired modified self protein; and

administering to the animal, an immunologically effective amount of the desired modified self-protein, wherein:

the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein, and,

the desired modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes, and B-cell autotolerance to the self-protein is broken; or,

n. preparing different modified self-proteins, wherein:

each modified self-protein is modified, in comparison to the self- protein, by containing a substitution of at least one peptide fragment of the self-protein with a peptide containing at least one immunodominant T-cell epitope which is foreign to the animal,

said substitution preserving secondary and tertiary structure of the self-protein, and

the different modified self-proteins differ from each other with respect to the position of the at least one immunodominant T-cell epitope;

ascertaining which of the different modified self-proteins elicits a desired specific neutralizing effect and thereby ascertaining a desired modified self protein; and

administering to the animal, an immunologically effective amount of the desired modified self-protein, wherein:

the self-protein is normally autotolerated by the animal and there is normally B-cell autotolerance by the animal to the self-protein, and,

the desired modified self-protein elicits antibodies that are against the self-protein, earlier and in higher titres, in comparison to the self-protein conjugated to a carrier protein or peptide containing T-cell epitopes, and B-cell autotolerance to the self-protein is broken].